

CARDIOVASCULAR MEDICINE

Detection of myocardial viability by dobutamine stress echocardiography: incremental value of diastolic wall thickness measurement

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Objective: To assess the diagnostic accuracy of baseline diastolic wall thickness (DWT) alone and as an adjunct to dobutamine stress echocardiography (DSE) for prediction of myocardial viability in patients with ischaemic left ventricular (LV) dysfunction, with the recovery of resting function after revascularisation as the yardstick.

Patients: 24 patients with ischaemic LV dysfunction (ejection fraction < 40%) scheduled for surgical revascularisation.

Setting: Regional cardiothoracic centre.

Methods: All patients underwent DSE before and resting echocardiography six months after revascularisation. DWT was measured in each of the 16 LV segments. A receiver operating characteristic (ROC) and a multi-ROC curve were generated to assess the ability of DWT alone and in combination with DSE to predict myocardial viability.

Results: DWT > 0.6 cm provided a sensitivity of 80%, a specificity of 51%, and a negative predictive value of 80% for the prediction of viability in akinetic segments. DSE had an excellent specificity (92%) but a modest sensitivity (60%) in akinetic segments. A combination of improvement at DSE or DWT > 0.8 cm improved sensitivity (90% v 60%, $p < 0.001$) and negative predictive value (92% v 78%, $p = 0.03$) in akinetic segments compared with DSE alone. This was achieved with some loss in specificity (75% v 92%, $p = 0.01$) and positive predictive value (71% v 82%, $p = 0.79$).

Conclusions: DWT measurement may improve the sensitivity of DSE for the detection of myocardial viability. Akinetic segments with DWT > 0.8 cm have a good chance of recovery despite the absence of contractile reserve during DSE. Further testing may be required before excluding myocardial viability in these cases.

The presence of myocardial viability in patients with severe ischaemic left ventricular (LV) dysfunction has major implications for management and prognosis.^{1,2} Among the several tests used, detection of contractile reserve during dobutamine infusion has emerged as a non-invasive, safe, and accurate method for the detection of viable myocardium.^{3,4} Myocardial thinning occurs in areas of myocardial necrosis^{5,6} and preserved diastolic wall thickness (DWT) in dysfunctional segments may therefore indicate significant myocardial viability. Regional DWT can be easily measured off line from the baseline images acquired during a routine dobutamine stress echocardiography (DSE) study, with no additional patient discomfort or cost. The present study assessed the diagnostic accuracy of baseline DWT measurement alone and as an adjunct to standard DSE for the prediction of segmental recovery of function at six months after revascularisation in patients with severe ischaemic LV dysfunction.

METHODS

The study group consisted of 24 patients with ischaemic LV dysfunction (ejection fraction < 40%) scheduled for coronary artery bypass grafting (CABG) at the Freeman Cardiothoracic Centre (table 1). Patients with a recent acute ischaemic event (< 6 weeks), coronary anatomy unsuitable for complete revascularisation, or inadequate image quality were not included. All patients underwent DSE at one week preoperatively and resting echocardiography at six months after CABG. The patients' medications, including β blockers, were not discontinued for the study.⁷ The studies performed did

not influence the decision to proceed with revascularisation. The hospital's ethics committee approved the study and informed consent was obtained from all patients.

Echocardiography

An ATL HDI 5000CV system was used and all studies were carried out with a single broadband transducer (3/2 MHz) and tissue harmonic imaging.⁸ DSE studies were performed as previously described.⁷ During analysis all DSE stages were considered for detection of contractile reserve, as the majority of patients were taking β blockers.^{7,9}

The standard 16 segment model¹⁰ was used for wall motion analysis and DWT measurement. All studies were interpreted in random order by a consensus of two experienced observers blinded to the patients' names and other clinical data. A wall motion score index was assigned to each stage of the test. Evidence of wall thickening in a previously akinetic segment or normalisation of thickening in a previously hypokinetic segment was regarded as the criterion of myocardial viability in the preoperative study. The same criteria were used to define recovery of resting segmental wall motion post-operatively. Evidence of hypokinesia, akinesia, or dyskinesia in a previously normokinetic segment or of akinesia or dyskinesia in a previously hypokinetic segment was considered the criterion of inducible ischaemia in the preoperative study. LV ejection fraction was calculated off line from

Abbreviations: AUC, area under the receiver operating characteristic curve; CABG, coronary artery bypass grafting; CI, confidence interval; DSE, dobutamine stress echocardiography; DWT, diastolic wall thickness; LV, left ventricular; ROC, receiver operating characteristic

Table 1 Clinical, angiographic, and operative data of study patients (n = 24)

	Number (%)
EF 25–40%	17 (71%)
EF <25%	7 (29%)
History of myocardial infarction	17 (71%)
Stable angina	17 (71%)
Dyspnoea (NYHA I–II)	7 (29%)
Dyspnoea (NYHA III–IV)	10 (42%)
Q waves on ECG	15 (63%)
Previous CABG	1 (4%)
Previous PTCA	1 (4%)
Diabetes	5 (21%)
Hypertension	14 (58%)
Hyperlipidaemia	20 (83%)
Smoking	15 (63%)
β Blockers	18 (75%)
Calcium blockers	9 (38%)
Long acting nitrates	7 (29%)
ACE inhibitors	18 (75%)
Diuretics	9 (38%)
Two vessel disease	3 (12%)
Three vessel disease	21 (88%)
Number of distal coronary anastomoses	
2	3 (12%)
3	5 (21%)
4	15 (63%)
5	1 (4%)

ACE, angiotensin converting enzyme; CABG, coronary artery bypass grafting; EF, ejection fraction; NYHA, New York Heart Association; PTCA, percutaneous coronary angioplasty.

the apical two and four chamber views by the standard Simpson's method.

DWT measurement

DWT was measured off line for each of the 16 LV segments by two observers blinded to the patients' names and clinical and DSE data. The resting preoperative end diastolic frames providing the best possible visualisation of the endocardial and epicardial borders were selected for analysis. The mean value (in centimetres) of three measurements from the leading endocardial edge to leading epicardial edge^{11, 12} was assigned to each segment. The intraobserver and interobserver variabilities were 0.04 (0.01) cm and 0.05 (0.02) cm, respectively.

Statistical analysis

To assess the ability of DWT to predict postoperative recovery of resting function, a receiver operating characteristic (ROC) curve was generated. The area under the ROC curve (AUC) along with the corresponding 95% confidence interval (CI) is reported. The sensitivity and specificity of DSE alone are reported with 95% CIs. Lastly, to assess whether combining the tests improved accuracy, a multi-ROC curve was generated for which the test variable was: (1) positive DSE test and positive DWT; or (2) positive DSE test or positive DWT. Akinetic and hypokinetic segments were then analysed separately.

RESULTS

Baseline echocardiography

Of 384 myocardial segments analysed, 248 (65%) were dysfunctional (114 hypokinetic and 134 akinetic). Accurate measurement of DWT was possible in 94% of all segments and in 96% of the dysfunctional segments. The mean (SD) DWT was significantly higher in normal than in dysfunctional segments (1.08 (0.29) cm *v* 0.83 (0.31) cm, $p < 0.001$). Hypokinetic segments had a higher DWT than did akinetic segments (0.92 (0.27) cm *v* 0.74 (0.32) cm, $p < 0.001$).

Dobutamine stress echocardiography

The full protocol was completed for 17 patients and was stopped at stages 3 and 4 for the remaining patients (achievement of target heart rate or evidence of inducible ischaemia). Mean (SD) heart rate was 65(18) beats/min at rest and increased to 96 (23) beats/min at peak stress. No significant adverse events occurred.

The response of the 248 dysfunctional segments to dobutamine was as follows: continuous improvement was observed in 84 segments (34%), biphasic response in 38 (15%), worsening in 8 (3%), and no change in 118 segments (48%). Dyskinesia at peak stress without improvement at low dose developed in 2% of the akinetic segments. In addition, deterioration of function was observed in 11% (15 of 136) of the segments that were normal at baseline. Evidence of myocardial viability (continuous improvement or biphasic response) was observed in 28% (38 of 134) of the akinetic segments and in 75% (85 of 114) of the hypokinetic segments. Thus, myocardial viability was detected more often in hypokinetic than in akinetic segments ($p < 0.001$).

Effect of coronary revascularisation on regional LV function

None of the patients had angina at six months after CABG. Mean (SD) resting wall motion score index decreased to 1.66 (0.41) *v* 2.00 (0.43) preoperatively ($p < 0.005$). Mean (SD) ejection fraction increased from 29 (8)% to 39 (12)% ($p < 0.005$). Of the 248 dysfunctional segments, 111 (45%) had improved function at the follow up study (fig 1). In particular, improved function was evident in 52 of the 134 akinetic segments (39%), 38 of which improved to hypokinesis and 14 to normal function. Of the 114 hypokinetic segments 59 (52%) resumed normal function after revascularisation. None of the three akinetic segments that became dyskinetic at peak stress without improvement at low dose recovered function after revascularisation.

Accuracy of DSE in predicting recovery of segmental resting LV function at six months after CABG

Of the 111 dysfunctional segments with improved function at follow up, 86 (77%) had also improved during DSE, whereas 93 of the 137 (68%) segments with no recovery of function had not improved during DSE. Improvement in akinetic segments during DSE had an excellent specificity but a modest sensitivity for recovery of resting function after CABG, whereas improvement in hypokinetic segments was more sensitive but less specific (table 2).

Accuracy of DWT in predicting recovery of segmental resting LV function at six months after CABG

Preoperative DWT was greater in myocardial segments with recovered resting function after CABG than in segments with no recovery (0.92 (0.32) *v* 0.75 (0.28) cm, $p < 0.001$). The AUC for DWT was 0.67 (95% CI 0.60 to 0.74, $p < 0.001$) for all dysfunctional segments, 0.53 (95% CI 0.42 to 0.64, $p = 0.624$) for hypokinetic segments, and 0.75 (95% CI 0.66 to 0.84, $p < 0.001$) for akinetic segments. Although the area was > 0.5 the excess predictive ability of DWT for hypokinetic segments was not significant. DWT measurement was therefore found to be useful for the prediction of recovery of function after CABG only in akinetic segments (table 3).

Combining DWT and DSE in predicting recovery of segmental resting LV function at six months after CABG

All segments

The AUC for DSE was 0.73 (95% CI 0.66 to 0.79) versus 0.67 (95% CI 0.60 to 0.70) for DWT. The sensitivity and specificity

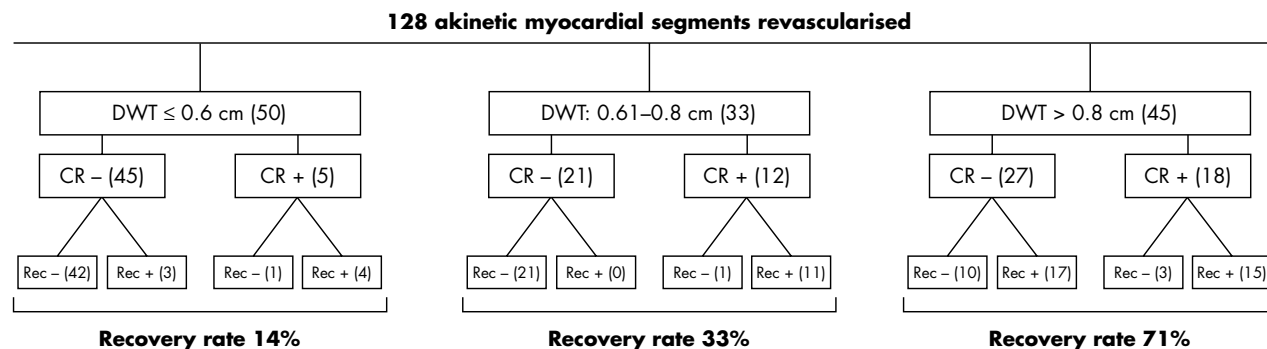


Figure 1 Chart showing the postoperative outcome of 128 revascularised akinetic segments grouped according to diastolic wall thickness (DWT) and response to dobutamine stress echocardiography. CR, contractile reserve; Rec, functional recovery.

of DSE in predicting recovery of resting function were 77% (95% CI 69% to 84%) and 68% (95% CI 60% to 75%), respectively. To achieve the same sensitivity with DWT as the test variable, the cut off required would be 0.73 cm. However, the corresponding specificity would be only 49%. The combination of DSE or DWT produced an AUC of 0.73 (95% CI 0.59 to 0.80, $p = 0.002$). The combination of DSE and DWT produced an AUC of 0.49 (95% CI 0.38 to 0.60, $p = 1.0$).

Hypokinetic segments

The AUC for DSE was 0.63 (95% CI 0.53 to 0.73) versus 0.53 (95% CI 0.42 to 0.64) for DWT. The combination of DSE or DWT produced an AUC of 0.26 (95% CI 0.09 to 0.56) and the combination of DSE and DWT produced an AUC of 0.53 (95% CI 0.40 to 0.65) indicating no incremental value of DWT in addition to DSE alone in hypokinetic segments.

Akinetic segments

The AUC for DSE was 0.76 (95% CI 0.67 to 0.85) versus 0.75 (95% CI 0.66 to 0.84) for DWT. The combination of DSE or DWT produced an area under the multi-ROC curve of 0.79 (95% CI 0.65 to 0.89) indicating a slight improvement compared with DSE alone. A combination of improvement at DSE or DWT > 0.8 cm significantly improved sensitivity (90% v 60%, $p < 0.001$) and negative predictive value (92% v 78%, $p = 0.03$) compared with DSE alone. This was achieved with the cost of some loss in specificity (75% v 92%, $p = 0.01$) and positive predictive value (71% v 82%, $p = 0.79$) (table 3).

DISCUSSION

Since the introduction of the concept of hibernating myocardium,^{13–14} several non-invasive tests have been extensively evaluated for their accuracy to predict functional recovery after revascularisation in patients with chronic ischaemic LV dysfunction.^{15–17} Among them, detection of contractile reserve during dobutamine infusion has emerged as a safe, non-invasive, and accurate method of identifying

viable myocardium and is the technique of first choice in many centres with available equipment and expertise for this method.^{4–18} Several previous studies^{19–21} have established, however, that DSE is highly specific but modestly sensitive for the prediction of functional recovery in akinetic segments. Thus, it is apparent that certain myocardial segments are resistant to dobutamine stimulation but eventually recover function after revascularisation and are therefore judged to be hibernating. Exhausted coronary flow reserve,²² myofibrillar loss,²³ and disruption of intercellular conduction²⁴ are some of the mechanisms proposed to explain the phenomenon of dobutamine resistant yet viable myocardium.

In patients with severe ischaemic LV dysfunction, the clinical decision to recommend revascularisation is based on the presence of myocardial viability and has major implications for management and prognosis. It is becoming increasingly clear, however, that more than one method for viability detection may be necessary at times to make the correct management decision in certain cases.

Myocardial thinning and increase in echoreflectivity are long known to occur in areas of scar tissue caused by chronic transmural myocardial infarction.^{5–6} More recently a normal DWT and acoustic reflectance were reported to predict viable myocardium²⁵ and a DWT of ≤ 0.6 cm was reported to virtually exclude viability²⁶ in patients with healed Q wave myocardial infarction. La Canna and colleagues¹² reported that a DWT < 0.5 cm on echocardiography was the best predictor of non-recovery of function in patients with chronic ischaemic LV dysfunction. Cwajg and colleagues¹¹ reported that DWT measurement can predict recovery of function in patients with suspected myocardial hibernation, similar to thallium-201 scintigraphy, and that a DWT of ≤ 0.6 cm practically excludes a relevant amount of viable myocardium.

Most previous reports have, however, focused mainly on the high predictive accuracy of reduced DWT to exclude any significant amount of myocardial viability. In the present study, and in agreement with the previous reports,^{11–12, 25–26} a DWT of ≤ 0.6 cm on baseline echocardiography excluded the presence of significant viability with a negative predictive

Table 2 Diagnostic accuracy of dobutamine stress echocardiography (DSE) in predicting recovery of segmental function at six months after CABG

	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
All segments	77 (69 to 84)	68 (60 to 75)	66 (58 to 74)	78 (71 to 85)	72 (66 to 78)
Akinetic	60 (46 to 72)	92 (83 to 96)	82 (67 to 91)	78 (69 to 85)	79 (72 to 86)
Hypokinetic	93 (84 to 97)	33 (22 to 45)	60 (50 to 69)	82 (62 to 93)	64 (55 to 73)
p Value	0.001	<0.001	0.03	0.99	0.03

95% confidence intervals are shown.

NPV, negative predictive value; PPV, positive predictive value.

Table 3 Accuracy of DSE, diastolic wall thickness (DWT), and their combination in predicting recovery of function at six months after CABG in akinetic segments

	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
DWT >0.6 cm	80 (68 to 89)	51 (40 to 62)	52 (41 to 63)	80 (66 to 89)
DWT >0.8 cm	61 (47 to 73)	78 (67 to 86)	65 (50 to 77)	75 (65 to 83)
DSE	60 (46 to 72)	92 (83 to 96)	82 (67 to 91)	78 (69 to 85)
DSE or DWT >0.6 cm	90 (79 to 96)	49 (38 to 60)	54 (44 to 64)	88 (76 to 95)
DSE or DWT >0.8 cm	90 (79 to 96)	75 (65 to 84)	71 (59 to 80)	92 (83 to 97)
DSE and DWT >0.6 cm	49 (36 to 62)	94 (86 to 97)	83 (66 to 93)	74 (64 to 81)

accuracy similar to that of DSE. However, in our study group DWT was ≤ 0.6 cm in only 39% of akinetic segments and > 0.8 cm in 35% of akinetic segments. We extended previous observations^{22–24} to hypothesise that the possible changes that render the hibernating myocardium non-responsive to dobutamine may occur at an earlier stage than the ultrastructural changes that lead to myocardial thinning. Indeed, myocardial segments with a DWT of > 0.8 cm had a recovery rate of 63% (17 of 27) despite the absence of inotropic response during DSE (fig 1). A DWT of > 0.8 cm as a single parameter produced a specificity of 78% and a positive predictive value of 65% for functional recovery in akinetic segments. The combination of DSE response or DWT > 0.8 cm produced the highest negative predictive accuracy (92%) with a good balance between sensitivity (90%) and specificity (75%) for functional recovery in akinetic segments.

In agreement with Elhendy and colleagues²⁷ we observed that akinetic segments that became dyskinetic at peak stress without improvement at low dose dobutamine did not recover function postoperatively. However, only 2% of akinetic segments had this type of response in our study group, probably due to the submaximal stress achieved.

In agreement with previous reports^{18–19, 28} and in contrast to akinetic segments, in this study DSE had high sensitivity but rather low specificity to predict recovery of resting function in hypokinetic segments. At rest, most LV wall thickening occurs as a result of endocardial thickening, and if the endocardium is necrosed resting function is diminished despite the presence of healthy tissue in the middle and outer myocardial layers.^{6, 29–30} In the present study DWT measurement had no excess predictive accuracy in addition to DSE in hypokinetic segments. Cwajg and colleagues¹¹ reported a significant improvement in specificity when the criterion of DWT of > 0.6 cm is added to DSE response in hypokinetic segments. However, myocardial segments with a DWT of < 0.6 cm are usually akinetic rather than hypokinetic,⁶ and as the authors explain this increase in specificity may be due to exclusion of thin, non-viable segments that exhibit tethering during DSE. Furthermore, hypokinesia indicates that most of the myocardium has escaped necrosis and is hence viable.³⁰ The presence of inducible ischaemia rather than viability is of clinical concern in these cases.

Study advantages and limitations

Functional recovery after revascularisation may be delayed, particularly in severely dysfunctional, akinetic myocardial segments. We therefore assessed functional outcome at six months after CABG, a time interval previously shown to be most appropriate.³¹

Accurate measurement of DWT requires good delineation of epicardial and endocardial borders and it is not feasible in certain patients who present technical difficulties. All studies were carried out with tissue harmonic imaging, previously shown to dramatically improve image quality and endocardial border delineation.⁸ Patients whose echocardiograms

were of inadequate quality, despite the use of harmonic imaging, were not included in the study.

The study group consisted of patients with chronic ischaemic LV dysfunction. Findings do not apply to patients with acute or recent myocardial infarction, in whom an increased DWT may indicate myocardial damage and interstitial oedema after reperfusion rather than the presence of myocardial viability.³²

Although angiography was not repeated at six months after CABG to assess graft patency, early graft function was assessed intraoperatively in 10 patients as a quality control of the effectiveness of revascularisation³³ and was found to be satisfactory.

Conclusions and clinical implications

Regional DWT can be easily measured during DSE with no additional patient discomfort or cost and is a valuable adjunct to DSE for the detection of hibernating myocardium.

A DWT of ≤ 0.6 cm on baseline echocardiography can exclude the presence of significant viability with a negative predictive accuracy similar to that of DSE. Absence of inotropic response to dobutamine in akinetic segments with a DWT of < 0.8 cm can exclude the presence of significant viability with an extremely high negative predictive accuracy. However, akinetic myocardial segments with a DWT of > 0.8 cm have a good chance of recovery even in the absence of contractile reserve during DSE. Further testing may be required before myocardial viability can be excluded in these cases.

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Impaired elastic properties of ascending aorta in patients with giant cell arteritis

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Objective: To investigate the elastic properties of the ascending aorta in untreated patients with giant cell arteritis compared with age and sex matched normal controls.

Methods: Distensibility of the ascending aorta and aortic strain were measured in 22 patients with a recent diagnosis of giant cell arteritis (documented by a positive temporal artery biopsy) before initiation corticosteroid treatment, and in 44 age and sex matched healthy subjects. Aortic distensibility was calculated as $2 \times [\text{pulsatile change in aortic diameter}] / [(\text{diastolic aortic diameter}) \times (\text{aortic pulse pressure})]$, and aortic strain as $[\text{pulsatile change in aortic diameter}] / [\text{diastolic aortic diameter}]$. Aortic diameters were measured by echocardiography. Aortic pressures were obtained by external sphygmomanometry.

Results: Distensibility of the ascending aorta and aortic strain were both lower in patients with giant cell arteritis than in the controls ($p < 0.01$). In the patients with giant cell arteritis, aortic distensibility was inversely correlated with white blood cell count ($p < 0.05$), but not with erythrocyte sedimentation rate or C reactive protein.

Conclusions: Compared with healthy subjects, aortic distensibility and aortic strain are decreased in patients with giant cell arteritis before initiation of corticosteroid treatment. There was an association between the degree of reduction of aortic distensibility and the white blood cell count in the patient group.

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